

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

REQUEST FOR ACCESS TO AN ABANDONED APPLICATION UNDER 37 CFR 1.14

Bring completed form to:

File Information Unit, Room 2E04
2900 Crystal Drive
Arlington, VA 22202-3514

Telephone: (703) 308-2733

In re Application of

Application Number

09/471 349

Filed

Aug 27, 2001

Paper No. 14

I hereby request access under 37 CFR 1.14(a)(1)(iv) to the application file record of the above-identified ABANDONED application, which is not within the file jacket of a pending Continued Prosecution Application (CPA) (37 CFR 1.53(d)) and which is identified in, or to which a benefit is claimed, in the following document (as shown in the attachment):

United States Patent Application Publication No. _____, page, _____ line _____.

United States Patent Number 7163 817, column _____, line, _____ or

WIPO Pub. No. _____, page _____, line _____.

Related Information About Access to Applications Maintained in the Image File Wrapper System (IFW) and Access to Pending Applications in General

A member of the public, acting without a power to inspect, cannot order applications maintained in the IFW system through the FIU. If the member of the public is entitled to a copy of the application file, then the file is made available through the Public Patent Application Information Retrieval system (Public PAIR) on the USPTO internet web site (www.uspto.gov). Terminals that allow access to Public PAIR are available in the Public Search Room. The member of the public may also be entitled to obtain a copy of all or part of the application file upon payment of the appropriate fee. Such copies must be purchased through the **Office of Public Records** upon payment of the appropriate fee (37 CFR 1.19(b)).

For published applications that are still pending, a member of the public may obtain a copy of:

the file contents; the pending application as originally filed; or any document in the file of the pending application.

For unpublished applications that are still pending:

- (1) If the benefit of the pending application is claimed under 35 U.S.C. 119(e), 120, 121, or 365 in another application that has: (a) issued as a U.S. patent, or (b) published as a statutory invention registration, a U.S. patent application publication, or an international patent application publication in accordance with PCT Article 21(2), a member of the public may obtain a copy of: the file contents; the pending application as originally filed; or any document in the file of the pending application.
- (2) If the application is incorporated by reference or otherwise identified in a U.S. patent, a statutory invention registration, a U.S. patent application publication, or an international patent application publication in accordance with PCT Article 21(2), a member of the public may obtain a copy of the pending application as originally filed.

Neim Phe

Signature

4-3-07

Date

Neim Phe

Typed or printed name

09/471 349

Registration Number, if applicable

201 919 1718

Telephone Number

FOR PTO USE ONLY

Approved by: SDUnit: File Information UnitRECEIVED
APR 03 2007

This collection of information is required by 37 CFR 1.11 and 1.14. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **BRING TO: File Information Unit, Room 2E04, 2900 Crystal Drive, Arlington, Virginia.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

14



US007163817B2

(12) **United States Patent**
Sahni et al.

(10) Patent No.: **US 7,163,817 B2**
(45) Date of Patent: **Jan. 16, 2007**

(54) **CLOT-SPECIFIC STREPTOKINASE
PROTEINS POSSESSING ALTERED
PLASMINOGEN ACTIVATION
CHARACTERISTICS AND A PROCESS FOR
THEIR PREPARATION**

5,434,073 A * 7/1995 Dawson et al. 435/216
5,772,996 A * 6/1998 Atkinson 424/94.4
6,054,312 A * 4/2000 Larocca et al. 435/320.1

FOREIGN PATENT DOCUMENTS

EP 0 397 366 11/1990
WO WO 91/17765 11/1991

OTHER PUBLICATIONS

Wishart et al, A single mutation converts a novel phosphotyrosine binding domain into a dual-specificity phosphatase. *J Biol Chem.* Nov. 10, 1995;270(45):26782-5.*
Witkowski et al, Conversion of a beta-ketoacyl synthase to a malonyl decarboxylase by replacement of the active-site cysteine with glutamine. *Biochemistry.* Sep. 7, 1999;38(36):11643-50.*
Goldstein et al, A chimeric streptokinase with unexpected fibrinolytic selectivity. *Thromb Haemost.* Sep. 1996;76(3):429-38.*
EMBL database ID No. HSFIBI Jul. 16, 1988 Gronostajski et al.*
U.S. Appl. No. 10/631,588 Sahni et al, filed Jul. 31, 2003. STIC in house alignment of SEQ ID No.: 2 and SEQ ID No.: 11.*
Kombliht et al., Primary structure of human fibronectin: differential splicing may generate at least 10 polypeptides from a single gene. *EMBO J.* Jul. 1985;4(7):1755-9.*
Banerjee et al, Streptokinase—a clinically useful thrombolytic agent. *Biotechnol Adv.* Feb. 2004;22(4):287-307. Review.*
Jackson et al, Active streptokinase from the cloned gene in *Streptococcus sanguis* is without the carboxy-terminal 32 residues. *Biochemistry.* Jan. 14, 1986;25(1):108-14.*
Johnson et al, Influence of primary sequence transpositions on the folding pathways of ribonuclease T1. *Biochemistry.* Aug. 6, 1996;35(31):10223-33.*
Galys et al, Identification of regions in interleukin-1 alpha important for activity. *FEBS J.* Oct. 15, 1993;268(29):22105-11.*
Whistock et al, Prediction of protein function from protein sequence and structure. *FEBS Rev Biophys.* Aug. 2003;36(3):307-40. Review.*
Lucas et al., The binding of human plasminogen to fibrin and fibrinogen. *J Biol Chem.* Apr. 10, 1983;258(7):4249-56.*
Williams et al., Solution structure of a pair of fibronectin type I modules with fibrin binding activity. *J Mol Biol.* Jan. 28, 1994;235(4):1302-11.*
Huston et al., Protein engineering of antibody binding sites: recovery of specific activity in an anti-digoxin single-chain Fv analogue produced in *Escherichia coli*. *Proc Natl Acad Sci U S A.* Aug. 1988;85(16):5879-83.*

(Continued)

(76) Inventors: **Girish Sahni**, Institute of Microbial Technology, Sector 39A, Union Territory of Chandigarh-160036 (IN); **Rajesh Kumar**, Institute of Microbial Technology, Sector 39A, Union Territory of Chandigarh-160036 (IN); **Chaiti Roy**, Institute of Microbial Technology, Sector 39A, Union Territory of Chandigarh-160036 (IN); **Kammaraj Rajagopal**, Institute of Microbial Technology, Sector 39A, Union Territory of Chandigarh-160036 (IN); **Deepak Nihalani**, Institute of Microbial Technology, Sector 39, Union Territory of Chandigarh-160036 (IN); **Vasudha Sundaram**, Institute of Microbial Technology, Sector 39A, Union Territory of Chandigarh-160036 (IN); **Mahavir Yadav**, Institute of Microbial Technology, Sector 39A, Union Territory of Chandigarh-160036 (IN)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/940,235**

(22) Filed: **Aug. 27, 2001**

(65) **Prior-Publication Data**

US 2003/0059921 A1 Mar. 27, 2003

Related U.S. Application Data

(63) Continuation of application No. 09/471,349, filed on Dec. 23, 1999, now abandoned.

(30) **Foreign Application Priority Data**

Dec. 24, 1998 (IN) 3825/DEL/98

(51) Int. Cl.
C12N 9/48 (2006.01)
C12P 21/00 (2006.01)
C12P 21/06 (2006.01)

(52) U.S. Cl. **435/212; 435/69.1; 435/69.6; 435/69.7; 435/70.1; 435/71.1**

(58) Field of Classification Search **435/216, 435/183**
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,026,772 A * 6/1991 Kobayashi et al. 525/54.1
5,151,412 A * 9/1992 Brown 514/8
5,187,098 A 2/1993 Malke et al. 435/320.1

Primary Examiner—Sheridan Swope
(74) **Attorney, Agent, or Firm**—Sughrue Mion, PLLC

(57) **ABSTRACT**

The invention disclosed herein provides clot specific streptokinase proteins possessing altered plasminogen characteristics, including enhanced fibrin selectivity. The kinetics of plasminogen activation by these proteins are distinct from those of natural streptokinase, in that there is a temporary delay or lag in the initial rate of catalytic conversion of plasminogen to plasmin. Also disclosed are processes for preparing the proteins.

3 Claims, 26 Drawing Sheets